

INTERNATIONAL SEARCH REPORT

International Application No

T/GB2004/002579

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07D495/04 A61K31/5513 A61K9/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07D A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, BIOSIS, EMBASE, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5 457 101 A (GREENWOOD BEVERLEY ET AL) 10 October 1995 (1995-10-10) example 3	1-5, 8-10, 12, 13, 15-34
X	WO 03/007912 A (DEKEMPER KURT DOUGLAS ; NAIL STEVEN L (US); FITES ALAN LEE (US); LILLY) 30 January 2003 (2003-01-30) claim 1	1-5, 8-13, 15-34
X	WO 02/094236 A (ALEXZA MOLECULAR DELIVERY CORP) 28 November 2002 (2002-11-28) page 2, paragraph 10 example 3	1-5, 22-34
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☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

° Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

* & * document member of the same patent family

Date of the actual completion of the international search

13 October 2004

Date of mailing of the international search report

27/10/2004

Name and mailing address of the ISA

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>CHUE PIERRE ET AL: "Dissolution profile, tolerability, and acceptability of the orally disintegrating olanzapine tablet in patients with schizophrenia." CANADIAN JOURNAL OF PSYCHIATRY. REVUE CANADIENNE DE PSYCHIATRIE. OCT 2002, vol. 47, no. 8, October 2002 (2002-10), pages 771-774, XP002300476 ISSN: 0706-7437 page 772, left-hand column</p>	<p>1-5, 8-10, 12-20, 22-34</p>
X	<p>DRUGS AND THERAPY BULLETIN, vol. 17, no. 4, April 2003 (2003-04), pages 1-4, XP002300477</p> <p>pages 1-2</p>	<p>1-5, 8-10, 12-20, 22-34</p>

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Patent document cited in search report		Publication date	Patent family member(s)	Publication date
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REC'D 26 OCT 2004

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From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

29/12

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY
(PCT Rule 43bis.1)

Date of mailing

(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION

See paragraph 2 below

International application No.
PCT/GB2004/002579International filing date (day/month/year)
15.06.2004Priority date (day/month/year)
18.06.2003International Patent Classification (IPC) or both national classification and IPC
C07D495/04, A61K31/5513, A61K9/00Applicant
GENERICS [UK] LIMITED

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:



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Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
☐ a sequence listing
☐ table(s) related to the sequence listing
 - b. format of material:
☐ in written format
☐ in computer readable form
 - c. time of filing/furnishing:
☐ contained in the international application as filed.
☐ filed together with the international application in computer readable form.
☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/GB2004/002579

Box No. II Priority

1. ☒ The following document has not been furnished:

☒ copy of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(a)).

☐ translation of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(b)).

Consequently it has not been possible to consider the validity of the priority claim. This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.

2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43*bis*.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary:

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application,
- ☒ claims Nos. 28-34

because:

- ☒ the said international application, or the said claims Nos. 28-34 relate to the following subject matter which does not require an international preliminary examination (*specify*):

see separate sheet

- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- ☐ no international search report has been established for the whole application or for said claims Nos.
- ☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:
 - the written form ☐ has not been furnished
 - ☐ does not comply with the standard
 - the computer readable form ☐ has not been furnished
 - ☐ does not comply with the standard
- ☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.
- ☐ See separate sheet for further details

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	1-34
	No: Claims	
Inventive step (IS)	Yes: Claims	1-34
	No: Claims	
Industrial applicability (IA)	Yes: Claims	1-27
	No: Claims	

2. Citations and explanations

see separate sheet

1) The present application relates to an amorphous form of olanzapine, methods for its preparation and its application in pharmaceutical formulations.

2) Cited documents:

D1: US-A-5 457 101 (GREENWOOD BEVERLEY ET AL) 10 October 1995 (1995-10-10)

D2: WO 03/007912 A (DEKEMPER KURT DOUGLAS ; NAIL STEVEN L (US); FITES ALAN LEE (US); LILLY) 30 January 2003 (2003-01-30)

D3: WO 02/094236 A (ALEXZA MOLECULAR DELIVERY CORP) 28 November 2002 (2002-11-28)

D4: CHUE PIERRE ET AL: "Dissolution profile, tolerability, and acceptability of the orally disintegrating olanzapine tablet in patients with schizophrenia." CANADIAN JOURNAL OF PSYCHIATRY. REVUE CANADIENNE DE PSYCHIATRIE. OCT 2002, vol. 47, no. 8, October 2002 (2002-10), pages 771-774, XP002300476 ISSN: 0706-7437

D5: DRUGS AND THERAPY BULLETIN, vol. 17, no. 4, April 2003 (2003-04), pages 1-4, XP002300477

3) Novelty

Document D1 already describes a freeze dried formulation of olanzapine for injection (see example 3), in which olanzapine may be presumed to be in amorphous form.

Document D2 describes similarly a freeze dried form of olanzapine, in particular for preparing injection-formulations, and explicitly mentions the amorphous form of the product (see claim 3).

Document D3 describes formulations for preparing aerosols of olanzapine, in which the agent is to present predominantly in the amorphous form (see page 20, see also example 3).

Documents D4 and D5 describe orally disintegrating tablets of lyophilized olanzapine, in which the olanzapine may be presumed to be in amorphous form.

In this context it is further observed that the method of claims 6-7 is not specifically described in documents D1-D5. It should however be noted that any melting point determination on known crystalline olanzapine will involve melting as defined in claim 6 with eventual subsequent cooling in line with claim 7

4) Inventive step

In as far as any subject-matter could be identified in the present application, no basis for an inventive step can at present be recognized.

In this context, it is noted that the relatively high Tg and stability of the amorphous form reported in the present application (see page 10) may not have been explicitly mentioned in the available prior art, but should not have surprised the person skilled in the art in view of the availability of commercial products such as mentioned in for instance D5.

5) Further observations

Claims 28-34 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).